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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,327	03/12/2007	Nariyoshi Shinomiya	VAN67 P-328A	7013

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EXAMINER	
WOLLENBERGER, LOUIS V	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
04/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,327	SHINOMIYA ET AL.	
	Examiner	Art Unit	
	Louis Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2008 and 13 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,38 and 48-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,38 and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/26/2006; 2/4/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions/Status

The previous communication acknowledged Applicant's election without traverse of Group I, claim(s) 1-20 and 38, drawn to an interfering RNA molecule having a sequence that is sufficiently complementary to a sequence of mRNA encoded by **human *c-met* (SEQ ID NO:1),** and to RNAi molecules, expression constructs, and vectors thereof, and to a method of use thereof for treating a *c-met* tumor or cancer in a subject. Also acknowledged was Applicant's further election of SEQ ID NO:15, "stable" expression vector, and si-hMet-Ad5^{221}.

With regard to claims 48 and 50, In the reply filed 2/13/2009 Applicant further elected "glioblastoma" tumor or cancer. The reply is fully responsive.

Applicant is hereby notified the restriction requirement as applied to claims 15 and 16 is withdrawn. Claim 15 is rejoined with the elected invention for examination on the merits.

Claims 1-20, 38, and 48-50 are pending and examined herein.

Sequences

Applicant's submission of a substitute sequence listing, filed 2/13/2009, is acknowledged. The listing has been accepted and entered into the application.

Claim Objections

Claims 9 and 11 are objected to because the claims are missing the word "molecule" after the limitation "said RNAi" in line 2 of the claims. Correction is requires.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 recites the limitation "The viral vector of claim 13" in line 1. There is insufficient antecedent basis for this limitation in the claim.

For purposes of this examination, claim 16 is considered to be drawn to the vector of claim 14.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-12, 14-17, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Martinez et al. (US 20040265230 A1).

As shown by the alignment below, Martinez et al. taught an siRNA comprising a instant SEQ ID NO:15 for inhibiting the expression of a human colon cancer gene such as c-met in colon cancer cells in vitro and in vivo (see paragraph 110, disclosure beginning at paragraph 237,

and Table 7). It is said the siRNAs can be expressed in vitro and in vivo from vectors using Pol III promoters (parag. 241). Recommended vectors include adenoviral and retroviral vectors (parag. 334). Compositions and methods of using said compositions comprising any of the disclosed siRNAs to treat colon cancer are also disclosed.

Accordingly, Martinez et al. anticipate the instantly claimed siRNAs and methods.

```
RESULT 1
US-10-751-736-6634
; Sequence 6634, Application US/10751736
; Publication No. US20040265230A1
; GENERAL INFORMATION:
;  APPLICANT: Wyeth
;  APPLICANT:  Martinez, Robert
;  APPLICANT:  Brown, Eugene
;  APPLICANT:  Liu, Wei
;  TITLE OF INVENTION: COMPOSITIONS AND METHODS FOR DIAGNOSING AND TREATING COLON
;  TITLE OF INVENTION:  CANCERS
;  FILE REFERENCE: AM100927 (031896-002000)
;  CURRENT APPLICATION NUMBER: US/10/751,736
;  CURRENT FILING DATE:  2003-01-06
;  PRIOR APPLICATION NUMBER: US Provisional Application 60/438,000
;  PRIOR FILING DATE: 2003-01-06
;  NUMBER OF SEQ ID NOS: 54873
;  SOFTWARE: PatentIn version 3.2
; SEQ ID NO 6634
;   LENGTH: 21
;   TYPE: DNA
;   ORGANISM: homo sapiens
US-10-751-736-6634

  Query Match             100.0%;  Score 19;  DB 10;  Length 21;
  Best Local Similarity   100.0%;  Pred. No. 32;
  Matches   19;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GTGCAGTATCCTCTGACAG 19
              |||||||||||||||||||
Db          3 GTGCAGTATCCTCTGACAG 21


RESULT 2
US-10-751-736-6635
; Sequence 6635, Application US/10751736
; Publication No. US20040265230A1
; GENERAL INFORMATION:
;  APPLICANT: Wyeth
;  APPLICANT:  Martinez, Robert
;  APPLICANT:  Brown, Eugene
;  APPLICANT:  Liu, Wei
;  TITLE OF INVENTION: COMPOSITIONS AND METHODS FOR DIAGNOSING AND TREATING COLON
;  TITLE OF INVENTION:  CANCERS
;  FILE REFERENCE: AM100927 (031896-002000)
;  CURRENT APPLICATION NUMBER: US/10/751,736
;  CURRENT FILING DATE:  2003-01-06
;  PRIOR APPLICATION NUMBER: US Provisional Application 60/438,000
;  PRIOR FILING DATE: 2003-01-06
;  NUMBER OF SEQ ID NOS: 54873
;  SOFTWARE: PatentIn version 3.2
; SEQ ID NO 6635
;   LENGTH: 21
;   TYPE: RNA
;   ORGANISM: RNAi
US-10-751-736-6635

  Query Match             100.0%;  Score 19;  DB 10;  Length 21;
  Best Local Similarity   73.7%;  Pred. No. 32;
  Matches   14;  Conservative    5;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GTGCAGTATCCTCTGACAG 19
              |:||||:|:|||:|:|||||
Db          1 GUGCAGUAUCCUCUGACAG 19
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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 8-18, 38, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mroczkowski et al. (EP 1 243 596 A2) in view of:

1. Abounader et al. (2002) *FASEB J.* 16(1):108-110;

2. Tuschl et al. (US 2004/0259247 A1);
3. Elbashir et al. et al. (2002) *Methods* 26:199-213;
4. Shi et al. (US 2003/0180756 A1); and
5. Kaemmerer (US 2004/0162255 A1).

As shown by Mroczkowski et al. and Abounader et al. the mRNA sequence corresponding to instant SEQ ID NO:1 encoding human c-met (hepatocyte growth factor receptor) was known in the prior art. See page 8 of Mroczkowski et al., showing the full length sequence and identifying the sequence as that of GenBank Acc. No. NM_000245; and see the report by Abounader et al., describing ribozyme sequences targeted to human c-met.

As further shown by Mroczkowski et al. and Abounader et al., the correlation between c-met expression and several different human carcinomas, including glioblastomas, was well established. Each had taught that inhibiting c-met expression inhibits and sometimes reverses cancer cell growth. See pages 2 and 3 in Mroczkowski et al., and entire disclosure of Abounader et al. More specifically, Abounader et al. showed the growth human glioblastoma cells in culture and in animals may be effectively inhibited using adenoviral expression constructs encoding ribozymes targeted to the human c-met gene. It is said, for example, treatment of animals bearing intracranial glioma xenografts with anti-SF/HGF and anti-c-met U1snRNA/ribozymes by either intratumoral injections of adenoviruses expressing the transgenes or intravenous injections of U1snRNA/ribozyme-liposome complexes substantially inhibited tumor growth and promoted animal survival.

Accordingly, one of skill would have had ample reason to make and use inhibitors of c-met expression, including any nucleic acid-based inhibitor, to further investigate the role of c-met in human cancers, identify drugs capable of inhibiting c-met function, and to effectively treat cancer in humans suffering from c-met dependent cancer. To this end, one of skill would have been motivated to make and use the most effective nucleic acid based inhibitors known and available at the time. These included short interfering RNAs, or siRNAs, which were well known in the prior art for their ease of use, potency, and utility for suppressing gene expression in cells in vitro and in vivo for both research and therapeutic purposes.

At the time of invention, selecting and designing short interfering RNAs for inhibiting the expression of any known gene in mammalian cells, either through direct transfection or by endogenous expression from a suitable vector, was well established, as evidenced by Elbashir et al. et al. and Tuschl et al. (see entire disclosures). Each reference teaches that, fundamentally, target-specificity depends on Watson-Crick base pairing to the target. Thus, the complete genus of all possible siRNAs is described by the sequence of the mRNA target. The genus is further narrowed by selecting those siRNAs that meet the criteria set forth by, for example, Elbashir et al., who taught a step-by-step procedure for selecting candidate siRNAs from a known mRNA sequence, wherein the siRNAs are selected from the ORF preferably 50 to 100 nt downstream of the start codon, avoiding the 5' and 3' UTRs and sequences close to the UTRs (page 202). The practitioner then searches for sequences of the type AA(N19)UU, choosing those that have G/C contents of approximately 50%, or at least between 32 and 79%. If there are no AA(N19)UU type sequences, other sequences of the type AA(N21) are also suitable. The final collection of candidate siRNAs is then BLASTed to select those having sequence specificity with the target

(page 201, 202, and Fig. 2). At page 201, Elbashir et al. et al. taught that, while selection of the targeted region is currently a trial-and-error process, there is a likelihood of 80-90% success given a large enough random selection of target genes. Accordingly, the prior art suggested that siRNAs designed in silico according to these basic rules could reasonably be expected to trigger sequence-specific RNAi in cells in culture. Thus, the scope and contents of the prior art suggests that one of skill would have readily envisioned the genus of candidate siRNAs satisfying these criteria for the human c-met sequence disclosed by Mroczkowski et al., i.e., GenBank NM_000245. (MPEP 2144.08).

Furthermore, Tuschl et al. taught that siRNAs have advantages over conventional antisense oligonucleotides and ribozymes. For example, at paragraph 148 it is said siRNAs are extraordinarily powerful reagents for mediating gene silencing and that siRNAs are effective at concentrations that are several orders of magnitude below the concentrations applied in conventional antisense or ribozyme gene targeting experiments.

Moreover, as shown by Abounader et al. and, in more detail, by Shi et al. methods and materials for making and using recombinant adenoviral (transient) and retroviral (stable) vectors, comprising Pol III promoters such as the U6 promoter, for the expression of short therapeutic nucleic acids such as ribozymes and short interfering RNAs in mammalian cells was also well established in the prior art as an effective means for suppressing the expression of virtually any known gene for research and therapeutic purposes. Abounader et al. specifically demonstrate the use of adenoviral constructs encoding ribozymes targeted to c-met for inhibiting the growth of glioblastoma cells in vitro and in vivo. Shi et al. provide a complete blueprint for preparing and using Pol III-driven adenoviral and retroviral expression vectors encoding short interfering

RNAs (see entire disclosure). The Ad5 replication-incompetent genome is expressly recommended (see paragraph 125 in Shi et al. and Materials and Methods in Abounader et al., citing the Ad5-based method of Vogelstein et al.).

As shown by Kaemmerer et al. and Abounader et al., methods for delivering siRNA-encoding adenoviral vectors and other vectors into the brains of patients for the knockdown of specific disease-associated genes were also well established and enabled by the prior art (see pages 10 and 11 of Kaemmerer et al. and Materials and Methods and Results sections in Abounader et al.).

Accordingly, the prior art clearly suggested the instantly claimed siRNAs for inhibiting c-met expression for both research and therapeutic purposes to treat cancer. In view of the disclosure by Abounader et al. showing that the inhibition of c-met expression in human glioblastoma cells effectively inhibits the growth of said cells in culture and in living animals, and in view of the known potency of short interfering RNAs for accomplishing the same function, one of skill would have reasonably predicted that direct infusion of siRNAs or adenoviral vectors encoding said siRNAs into the brains of patients with glioblastoma cells would, similarly, result in the inhibition of glioblastoma cells in said patients thereby providing for a treatment of a human cancer. Moreover, in view Mroczkowski et al., one of skill would have further been motivated to make and use c-met siRNAs and vectors thereof to further investigate the role of c-met in several other types of human cancers in cells in vitro and in vivo, and perhaps develop strategies to treat such cancers and improve the human condition, obtaining all the known advantages of adenoviral and retroviral expression, including stable and long term expression.

Thus, in view of the scope and contents of the prior art as a whole, the instantly claimed invention would have been prima facie obvious to one of skill in the art at the time of invention.

***

Claims 19, 20, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martinez et al. (US 2004/0265230 A1) as applied to claims 1-12, 14-17, and 38 above, and further in view of Shi et al. (US 2003/0180756 A1) and Abounader et al. (2002) *FASEB J.* 16(1):108-110.

Martinez et al. is relied on for the reasons given above in the rejection under 35 USC 102.

While Martinez et al. teaches the use of adenoviral vectors in general, Martinez et al. does not teach Ad5 vectors in particular. Martinez et al. also does not teach using siRNAs targeted to c-met to treat glioblastoma.

Nevertheless, it would have been obvious to use any adenoviral vector known in the art to be suitable for the expression of short interfering RNAs to clone and express any of the siRNAs disclosed by Martinez et al. for suppressing c-met expression and function in cells in vitro and vivo for either research or therapeutic purposes to obtain all the benefits thereof such as effectively inhibiting glioblastoma cell growth in an individual in the same manner taught by Abounader et al.

As explained above in the rejection under 35 USC 103, Shi et al. taught methods and materials for making U6 Pol III-driven Ad5-based vectors for expressing short interfering RNAs in mammalian cells. Therefore, it would have been prima facie obvious to use the adenoviral-

based expression method of Shi et al. to express any of the siRNAs disclosed by Martinez et al., including the siRNA disclosed therein comprising SEQ ID NO:6634 or 6635, which comprises instant SEQ ID NO:15 to obtain the benefits of stable and long term expression associated with viral expression.

As shown by Abounader et al., ribozyme-mediated cleavage of c-met mRNA inhibits glioblastoma cell growth and possible metastasis. In view of the known potency of siRNAs, it would therefore have been obvious to make and use siRNAs targeting c-met (HGF) to achieve the same result and possibly obtain improved results with siRNA-mediated knockdown of c-met, which one of skill would reasonably expect.

Accordingly, in view of the scope and contents of the prior art, represented herein by the instantly cited references, the instant products and methods would have been prima facie obvious to one of skill at the time of invention.

***

Claims 1-20, 38, and 48-50 are rejected under 35 U.S.C. 103(a) as being obvious over Vande Woude et al. (US 2007/0020234 A1) in view of:

1. Martinez et al. (US 20040265230 A1).
2. Mroczkowski et al. (EP 1 243 596 A2) in view of:
3. Abounader et al. (2002) *FASEB J.* 16(1):108-110;
4. Tuschl et al. (US 2004/0259247 A1);
5. Elbashir et al. et al. (2002) *Methods* 26:199-213;
6. Shi et al. (US 2003/0180756 A1); and
7. Kaemmerer (US 2004/0162255 A1).

The applied reference, Vande Woude et al., has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Vande Woude et al. taught methods and materials for making and using met siRNA and vectors thereof for inhibiting the expression of human hepatocyte growth factor receptor (met) in human tumor cells and treating subjects thereby (paragraphs 4, 12, 28, and 84; and see pages 7-10)). It is said the interfering RNAs may be expressed from recombinant Pol III-based expression constructs, including Ad5 vectors (paragraphs 84, 94, 97). A preferred Ad5 constructs is said to be si-hMet-Ad5^{221} (paragraph 86), and which is said to have the strongest effect on human glioblastoma cells. Methods and materials for making and using siRNAs and viral vectors encoding siRNAs targeting *met* and other genes are disclosed at pages 7-10.

While Vande Woude et al. do not teach SEQ ID NO:15 specifically, the si-hMet-Ad5[221] vector would appear to be one encoding an siRNA comprising SEQ ID NO:15. Furthermore, the anti-c-met siRNA comprising SEQ ID NO:15 was known in the prior art as were as shown by Martinez et al., which is relied on for the reasons given above in the rejection under 35 USC 102. Moreover, methods and materials for making and using siRNAs targeted to human *c-met* and retroviral and adenoviral (including Ad5) vectors encoding siRNAs were well established in the prior art, as shown by at least References 1-7 above, each of which is relied on for the reasons given above in the rejection under 35 USC 103. As further shown by the combination of prior art references as a whole, methods for delivering adenoviral constructs encoding siRNAs into tissues and cells in the brain for treatment of specific diseases was also well established and routine (see Kaemmer, who taught direct delivery of siRNA into cells in the brain).

Finally, as shown by the prior art as a whole, represented herein by References 1-7, it was well known that the suppression of *c-met* expression could effectively inhibit cancer cell growth, particularly glioblastoma cell growth, and therefore could be used to treat such cancers in vivo.

Altogther, then, one of skill would have recognized the instantly claimed siRNAs and methods of use thereof were prima facie obvious over those siRNAs and methods disclosed by Vande Woude et al. in view of the knowledge and level of skill in the art at the time. The ordinary artisan would have had ample reason to use the siRNAs and adenoviral vectors disclosed therein to effectively inhibit c-met expression in human cancer cells to further investigate c-met function, develop therapeutic protocols, and treat c-met dependent cancers in affected individuals.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-20, 38, and 48-50 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over at least claims 9, 10, 22, 30, and 32 of copending Application No. 10/563,616 in view of:

1. Martinez et al. (US 20040265230 A1).
2. Mroczkowski et al. (EP 1 243 596 A2) in view of:
3. Abounader et al. (2002) *FASEB J.* 16(1):108-110;
4. Tuschl et al. (US 2004/0259247 A1);
5. Elbashir et al. et al. (2002) *Methods* 26:199-213;
6. Shi et al. (US 2003/0180756 A1); and

7. Kaemmerer (US 2004/0162255 A1).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting application claims a method for inhibiting tumor angiogenesis comprising providing a met (HGF/SF)-specific siRNA. The implicit purpose of the method is to inhibit tumor cell growth in an individual.

While the conflicting application does not specifically claim adenoviral or retroviral vectors encoding c-met siRNA or an siRNA comprising SEQ ID NO:15, these elements were known in and/or suggested by the prior art, as shown by References 1-7 above, which are relied on for the reasons given above in the rejections under 35 USC 102 and 103, and which as a whole taught the instantly claimed siRNAs, vectors, and methods.

Therefore, in view of the knowledge in the prior art, teaching the use of c-met siRNA to inhibit a variety of different cancers and showing how such siRNAs may be expressed from Pol III viral vectors, one of ordinary skill in the art would conclude that the invention defined in the claims at issue is anticipated by, or would have been an obvious variation of, the invention defined in a claim in the conflicting application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis Wollenberger whose telephone number is (571)272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/
Primary Examiner, Art Unit 1635
March 20, 2009